

R_M is hydroxy, alkoxy, substituted alkoxy or OR^p ;

R_N is hydrogen, R^p , alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, or $-C(X)-NR_tR_s$; wherein X is $=O$ or $=S$;

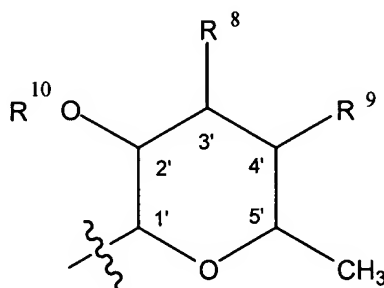
provided that Z and W cannot both simultaneously be, $>C=O$, $>CH_2$,

$>CH-NR_tR_s$, $>N-R_N$ or $>C=N-R_M$ or a bond,

U and Y independently are hydrogen, halogen, alkyl, or hydroxyalkyl;

R^1 is hydroxy, OR^p , $-O-S^2$ group or an $=O$;

S^1 is a sugar moiety of formula:



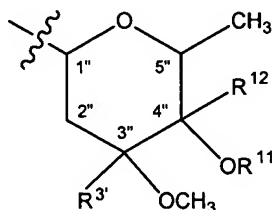
wherein

R^8 and R^9 are both hydrogen or together form a bond, or R^9 is hydrogen and R^8 is $-N(CH_3)R^y$, wherein

R^y is R^p , R^z or $-C(O)R^z$ wherein R^z is hydrogen or alkyl or alkenyl or alkynyl or cycloalkyl or aryl or heteroaryl or alkyl substituted with C_2 - C_7 -alkyl, C_2 - C_7 -alkenyl, C_2 - C_7 -alkynyl, aryl or heteroaryl

R^{10} is hydrogen or R^p ;

S^2 is a sugar moiety of formula :



wherein:

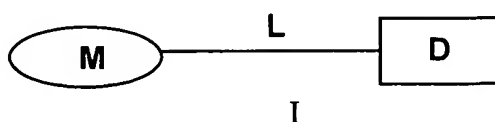
$R^{3'}$ is hydrogen or methyl;

chromoglycate, cinmetacin, clindanac, clopirac, sodium diclofenac, diflunisal, ditazol, droxicam, enfenamic acid, etodolac, etofenamate, felbinac, fenbufen, fenclozic acid, fendosal, fenoprofen, fentiazac, fepradinol, flufenac, flufenamic acid, flunixin, flunoxaprofen, flurbiprofen, glutametacin, glycol salicylate, ibufenac, ibuprofen, ibuproxam, indomethacin, indoprofen, isofezolac, isoxepac, isoxicam, ketoprofen, ketorolac, lornoxicam, loxoprofen, meclofenamic acid, mefenamic acid, meloxicam, mesalamine, metiazinic acid, mofezolac, montelukast, nabumetone, naproxen, niflumic acid, nimesulide, olsalazine, oxaceprol, oxaprozin, oxyphenbutazone, paracetamol, parsalimide, perisoxal, phenyl-acethyl-salicylate, phenylbutazone, phenylsalicylate, pyrazolac, piroxicam, pirprofen, pranoprofen, protizinic acid, reserveratol, salacetamide, salicylamide, salicylamide-O-acetyl acid, salicylsulphuric acid, salicin, salicylamide, salsalate, sulindac, suprofen, suxibutazone, tamoxifen, tenoxicam, tiaprofenic acid, tiaramide, ticlopridine, tinoridine, tolfenamic acid, tolmetin, tropesin, xenbucin, ximoprofen, zaltoprofen, zomepirac, tomoxiprol, zafirlukast and cyclosporin;

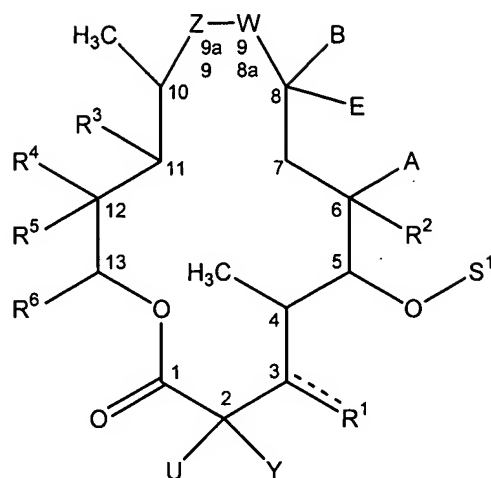
L is a linker molecule to which each of **M** and **D** are covalently linked; and

~~pharmaceutically acceptable salts and solvates thereof and individual diastereoisomers thereof~~ or a pharmaceutically acceptable salt or solvate thereof, or an individual diastereoisomer thereof.

2. (Currently Amended) A compound of the Formula I



wherein **M** represents a group of
Formula II:

**II**

wherein:

Z and W independently are: $>C=O$, $>CH_2$, $>CH-NR_tR_s$, $>N-R_N$ or $>C=N-R_M$ or a bond

wherein:

R_t and R_s independently are hydrogen or alkyl;

R_M is hydroxy, alkoxy, substituted alkoxy or OR^p ;

R_N is hydrogen, R^p , alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, or $-C(X)-NR_tR_s$; wherein X is $=O$ or $=S$;

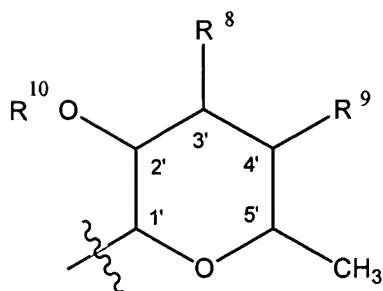
provided that Z and W cannot both simultaneously be, $>C=O$, $>CH_2$,

$>CH-NR_tR_s$, $>N-R_N$ or $>C=N-R_M$ or a bond,

U and Y independently are hydrogen, halogen, alkyl, or hydroxyalkyl;

R^1 is hydroxy, OR^p , $-O-S^2$ group or an $=O$;

S^1 is a sugar moiety of formula:



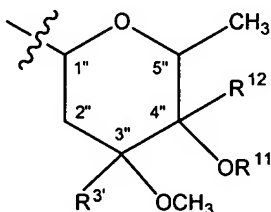
wherein

R^8 and R^9 are both hydrogen or together form a bond, or R^9 is hydrogen and R^8 is -
 $N(CH_3)R^y$, wherein

R^y is R^p , R^z or $-C(O)R^z$ wherein R^z is hydrogen or alkyl or alkenyl or alkynyl or
 cycloalkyl or aryl or heteroaryl or alkyl substituted with C_2 - C_7 -alkyl, C_2 - C_7 -
 alkenyl, C_2 - C_7 -alkynyl, aryl or heteroaryl

R^{10} is hydrogen or R^p ;

S^2 is a sugar moiety of formula :



wherein:

$R^{3'}$ is hydrogen or methyl;

R^{11} is hydrogen, R^p or $O-R^{11}$ is a group that with R^{12} and with C/4'' carbon atom forms a
 $>C=O$ or epoxy group;

R^{12} is hydrogen or a group that with $O-R^{11}$ group and with C/4'' carbon atom forms a
 $>C=O$ or epoxy group;

R^2 is hydrogen, hydroxy, OR^p or alkoxy

A is hydrogen or methyl;

B is methyl or epoxy;

E is hydrogen or halogen;

R^3 is hydroxy, OR^p , alkoxy or R^3 is a group that with R^5 and with C/11 and C/12 carbon
 atoms forms a cyclic carbonate or carbamate; or if W or Z is $>N-R_N$ R^3 is a group that with W or Z
 forms a cyclic carbamate;

R^4 is C_1 - C_4 alkyl;

R^5 is hydrogen, hydroxy, OR^P , C_1 - C_4 -alkoxy, or a group that with R^3 and with $C/11$ and $C/12$ carbon atoms forms a cyclic carbonate or carbamate;

R^6 is hydrogen or C_1 - C_4 -alkyl;

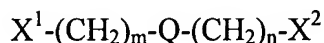
wherein **M** has a linkage site through which it is linked to **D** *via* linking group **L**; provided that the linkage site being at one or more of the following:

- a) any reactive hydroxy, nitrogen, or epoxy group located on S^1 , S^2 , or an aglycone oxygen if S^1 or/and S^2 is cleaved off;
- b) a reactive $>N-R_N$ or $-NR_tR_s$ or $=O$ group located on **Z** or **W**;
- c) a reactive hydroxy group located at any one of R^1 , R^2 , R^3 , and R^5 ;
- d) any other group that can be first derivatized to a hydroxy or $-NR_tR_s$ group and

R^P is hydroxyl or amino protective group;

wherein **L** represents a group of

Formula IV:



IV

wherein

X^1 is selected from: $-CH_2-$, $-C(O)-$, $OC(O)-$, $N-O-$ or $-OC(O)NH-$, $-C(O)NH-$;

X^2 is $-NH-$ or $-NHC(O)-$, $-OC(O)-$, $-C(O)-$, $-O$ or $-CH_2-$;

Q is $-NH-$ or $-CH_2-$, or absent;

wherein each $-CH_2-$ or $-NH-$ group may be optionally substituted by C_1 - C_7 -alkyl,

C_2 - C_7 -alkenyl, C_2 - C_7 -alkynyl, $C(O)R^x$, $C(O)OR^x$, $C(O)NHR^x$ wherein R^x ~~may be~~ is C_1 - C_7 -alkyl, aryl or heteroaryl;

the symbols m and n independently are a whole number from 0 to 4, with the proviso that if Q is NH, n cannot be 0

wherein D is derived from the NSAIDs selecting from the group consisting of: aceclofenac, acemetacin, acetaminophen, acetaminosalol, acetyl-salicylic acid, acetyl-salicylic-2-amino-4-picoline-acid, 5-aminoacetylsalicylic acid, alclofenac, aminoprofen, amfenac, ampyrone, ampiroxicam, anileridine, bendazac, benoxaprofen, bermoprofen, α -bisabolol, bromfenac, 5-bromosalicylic acid acetate, bromosaligenin, bucloxic acid, butibufen, carprofen, celexocib, chromoglycate, cinmetacin, clindanac, clopirac, sodium diclofenac, diflunisal, ditazol, droxicam, enfenamic acid, etodolac, etofenamate, felbinac, fenbufen, fenclozic acid, fendosal, fenoprofen, fentiazac, fepradinol, flufenac, flufenamic acid, flunixin, flunoxaprofen, flurbiprofen, glutametacin, glycol salicylate, ibufenac, ibuprofen, ibuproxam, indomethacin, indoprofen, isofezolac, isoxepac, isoxicam, ketoprofen, ketorolac, lornoxicam, loxoprofen, meclofenamic acid, mefenamic acid, meloxicam, mesalamine, metiazinic acid, mofezolac, montelukast, nabumetone, naproxen, niflumic acid, nimesulide, olsalazine, oxaceprol, oxaprozin, oxyphenbutazone, paracetamol, parsalimide, perisoxal, phenyl-acethyl-salicylate, phenylbutazone, phenylsalicylate, pyrazolac, piroxicam, pirprofen, pranoprofen, protizinic acid, reserveratol, salacetamide, salicylamide, salicylamide-O-acetyl acid, salicylsulphuric acid, salicin, salicylamide, salsalate, sulindac, suprofen, suxibutazone, tamoxifen, tenoxicam, tiaprofenic acid, tiaramide, ticlopridine, tinoridine, tolfenamic acid, tolmetin, tropesin, xenbucin, ximoprofen, zaltoprofen, zomepirac, tomoxiprol, zafirlukast and cyclosporin;

~~and a pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

3. (Canceled)

4. (Canceled)

5. (Previously Presented) A compound according to claim 2 wherein Z and W together are: -N(CH₃)-CH₂-, -NH-CH₂-, -CH₂-NH-, -C(O)-NH- or -NH-C(O)-;

A and B are methyl;

E is hydrogen;

R² is hydroxy or methoxy;

S¹ represents desosamine sugar wherein R⁸ is selected from: hydrogen, methyl,

amino, C₁-C₆ alkylamino or C₁-C₆ dialkylamino;

R⁹ and R¹⁰ are hydrogen;

R¹ is hydroxy or the O-S² group wherein the S² represents a cladinose sugar wherein:

R¹¹ is hydrogen, or O-R¹¹ is a group that with R¹² and with C/4" carbon atom forms a >C=O

or epoxy group; R¹² is hydrogen or a group that with O-R¹¹ and with C/4" carbon atom

forms a >C=O or epoxy group;

R¹³ is methyl;

U is hydrogen

Y is methyl;

R₆ is hydroxy, methyl or ethyl;

R⁵ is hydrogen, hydroxy, methoxy or a group that with R³ and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate bridge;

R³ is hydroxy or a group that forms a cyclic carbamate bridge with W or Z, or R³ is a group that with R⁵ and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate bridge;

R⁴ is methyl;

provided that the linkage is through the nitrogen of Z at N/9a position or through the carbon of R¹² or through the oxygen of R¹¹ both at C/4" position of the S² sugar.

6. (Previously Presented) A compound according to claim 2 wherein

X¹ is -CH₂- or -OC(O)-;

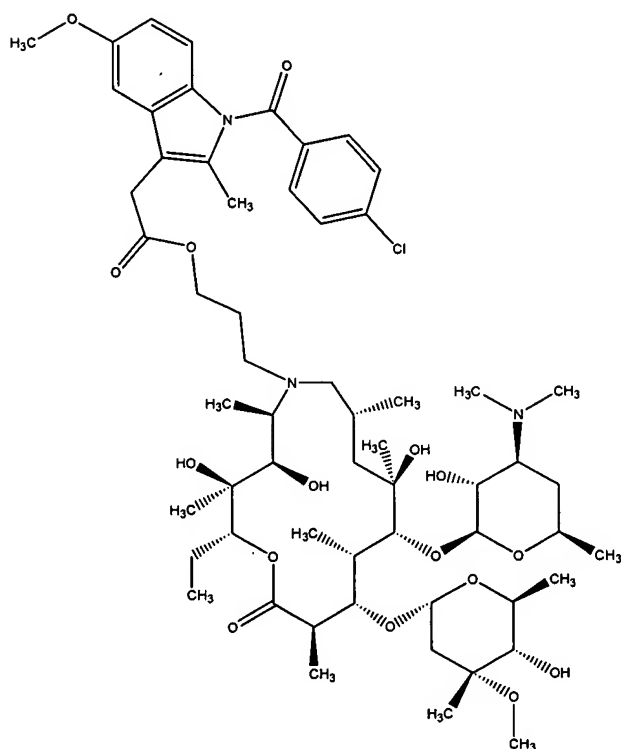
X² is -NHC(O)-;

Q is -NH- or absent.

7. (Previously Presented) A compound according to claim 2 wherein

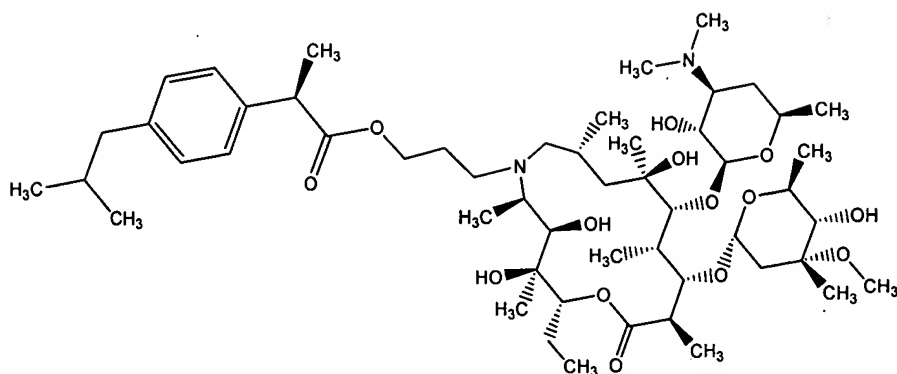
D is derived from a NSAID selecting from the group consisting of: S-(+) - ibuprofen, indomethacin, flurbiprofen, naproxen, ketoprofen, acetyl salicylic acid, sulindac, etodolac, ketorolac, suprofen, flunixin, diclofenac sodium and tolmetin sodium.

8. (Currently Amended) A compound of the formula



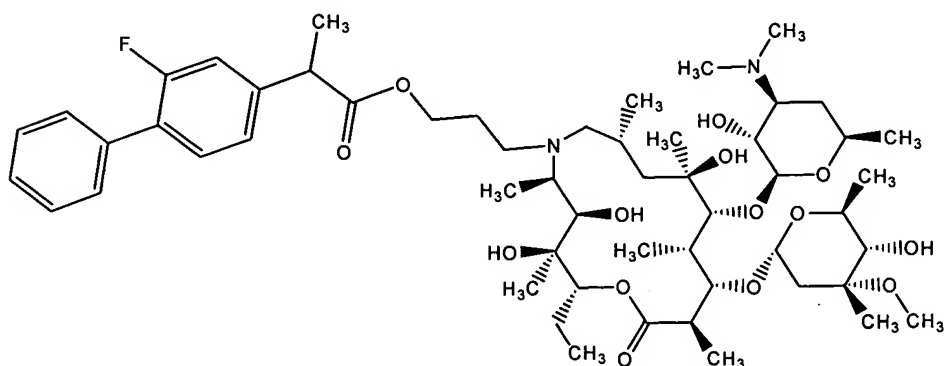
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

9. (Currently Amended) A compound of the formula



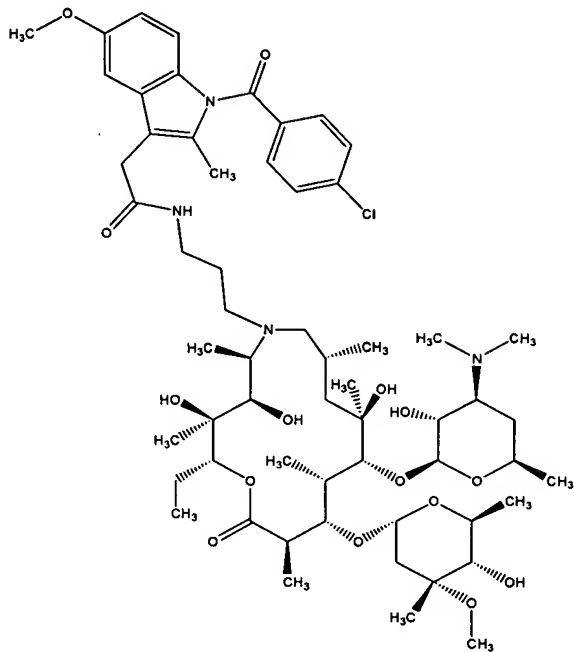
and pharmaceutically acceptable salts and solvates thereof or a pharmaceutically acceptable salt or solvate thereof.

10. (Currently Amended) A compound of the formula



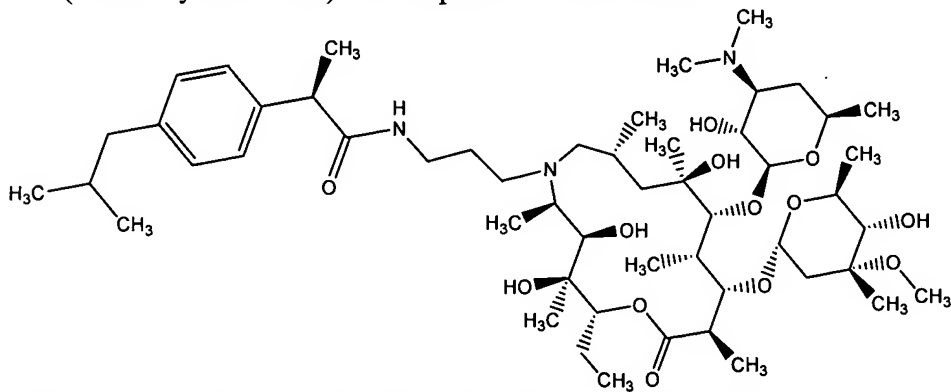
and pharmaceutically acceptable salts and solvates thereof or a pharmaceutically acceptable salt or solvate thereof.

11. (Currently Amended) A compound of the formula



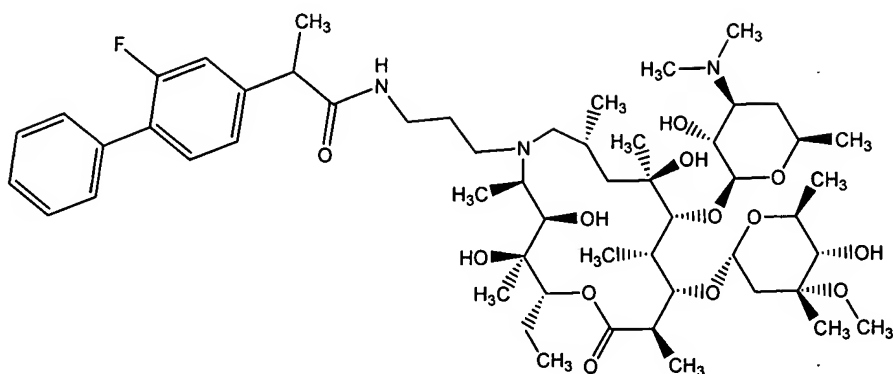
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

12. (Currently Amended) A compound of the formula



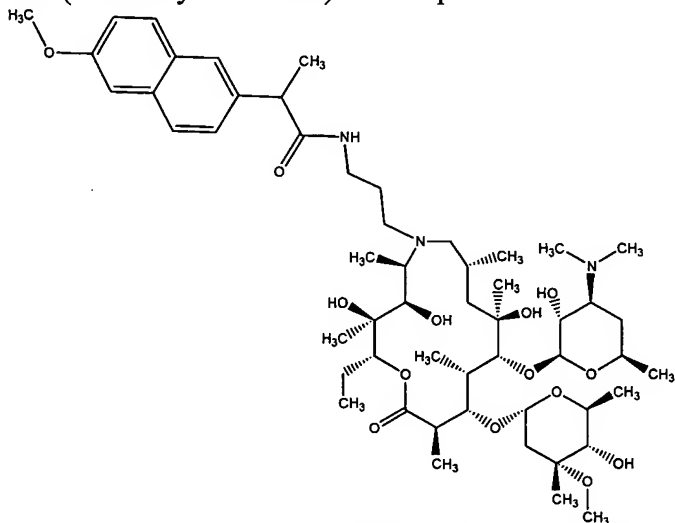
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

13. (Currently Amended) A compound of the formula



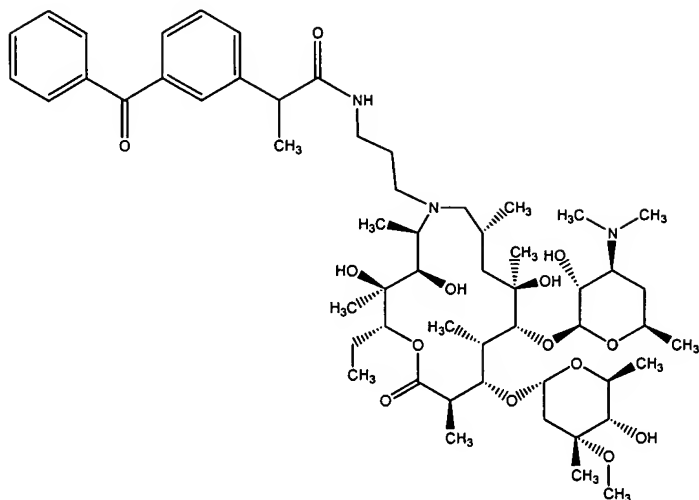
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

14. (Currently Amended) A compound of the formula



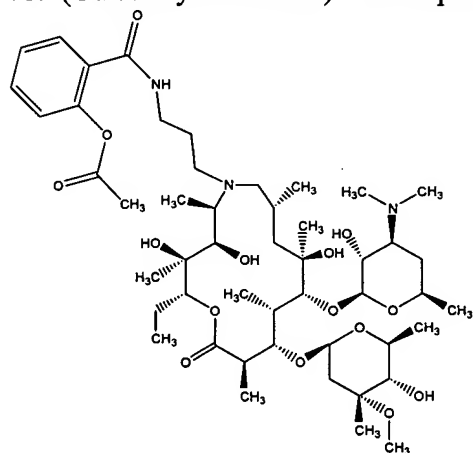
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

15. (Currently Amended) A compound of the formula



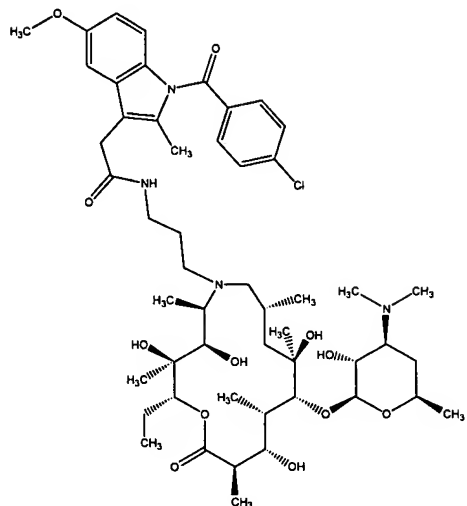
and pharmaceutically acceptable salts and solvates thereof or a pharmaceutically acceptable salt or solvate thereof.

16. (Currently Amended) A compound of the formula



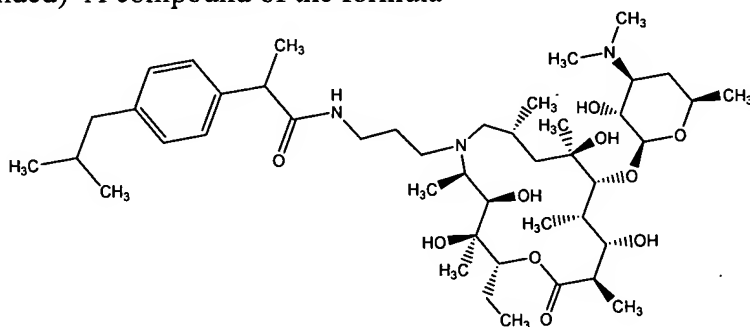
and pharmaceutically acceptable salts and solvates thereof or a pharmaceutically acceptable salt or solvate thereof.

17. (Currently Amended) A compound of the formula



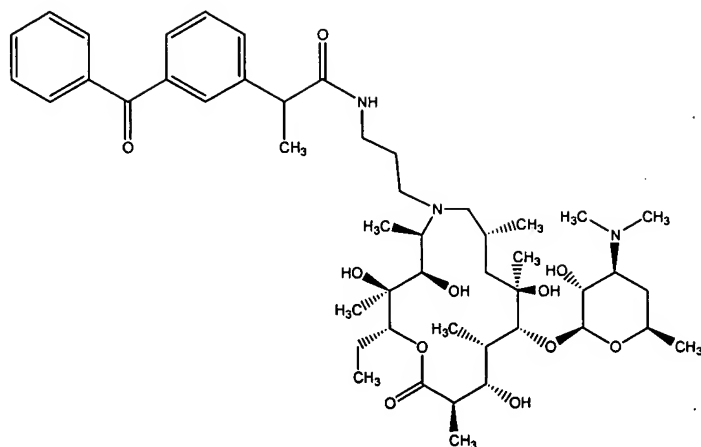
and pharmaceutically acceptable salts and solvates thereof or a pharmaceutically acceptable salt or solvate thereof.

18. (Currently Amended) A compound of the formula



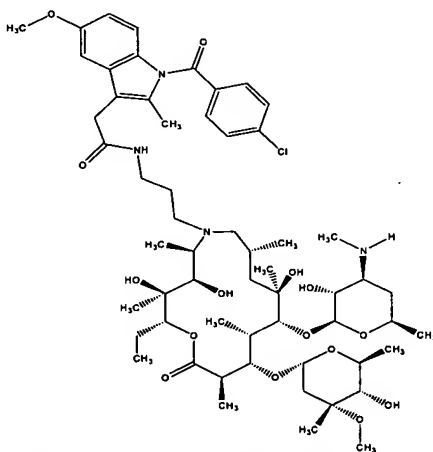
and pharmaceutically acceptable salts and solvates thereof or a pharmaceutically acceptable salt or solvate thereof.

19. (Currently Amended) A compound of the formula



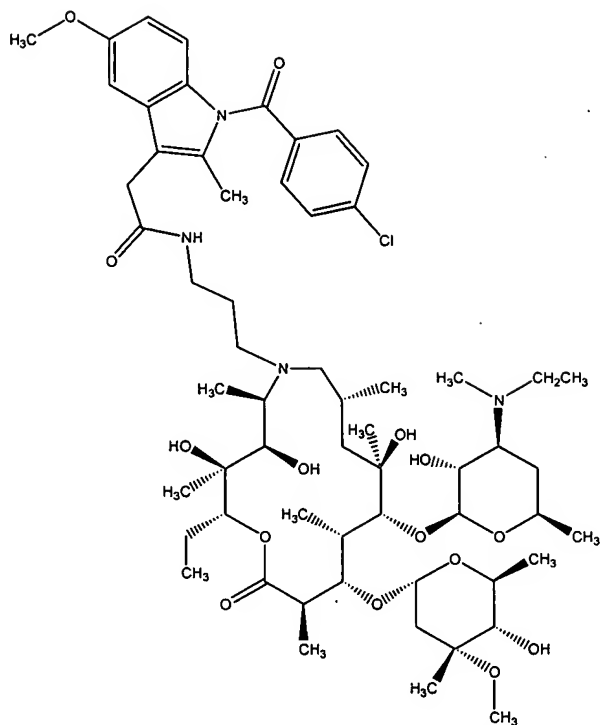
and pharmaceutically acceptable salts and solvates thereof or a pharmaceutically acceptable salt or solvate thereof.

20. (Currently Amended) A compound of the formula



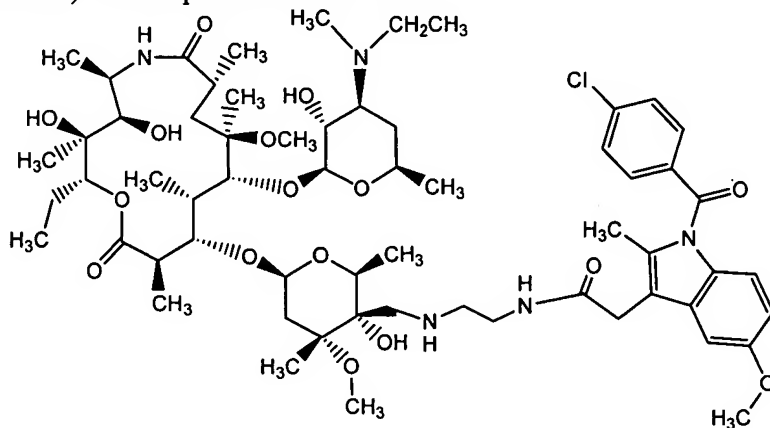
and pharmaceutically acceptable salts and solvates thereof or a pharmaceutically acceptable salt or solvate thereof.

21. (Currently Amended) A compound of the formula



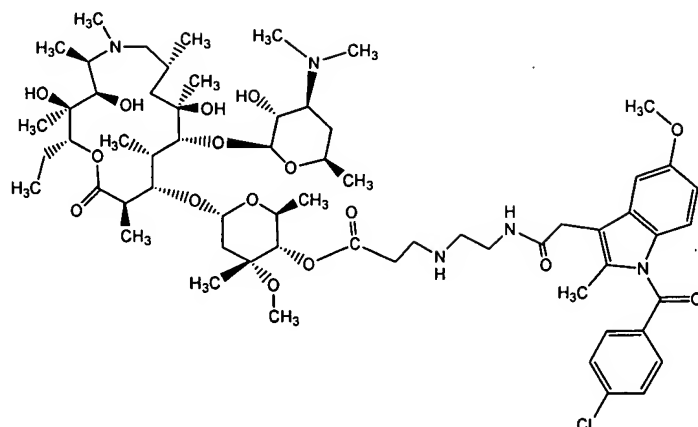
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

22. (Currently Amended) A compound of the formula



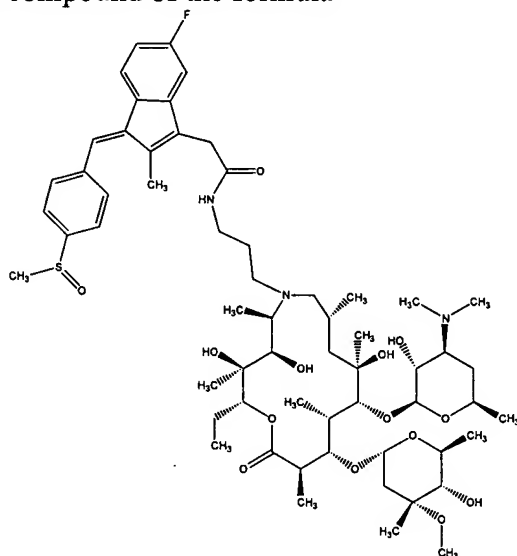
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

23. (Currently Amended) A compound of the formula



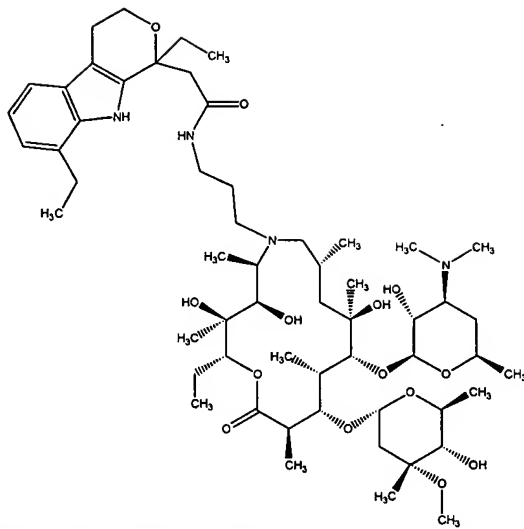
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

24. (Currently Amended) A compound of the formula



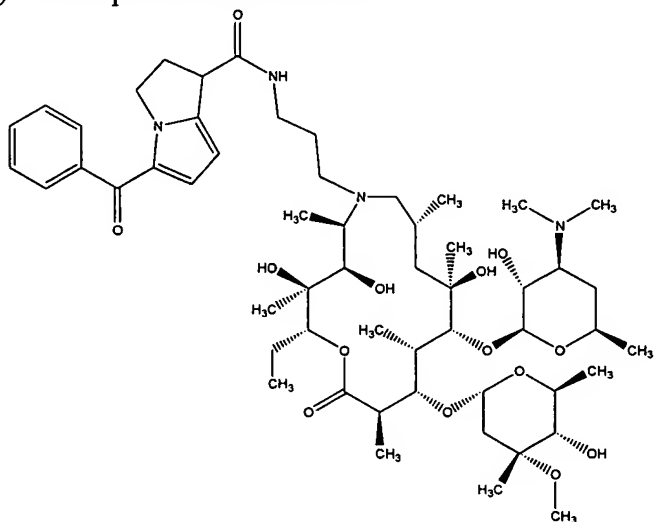
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

25. (Currently Amended) A compound of the formula



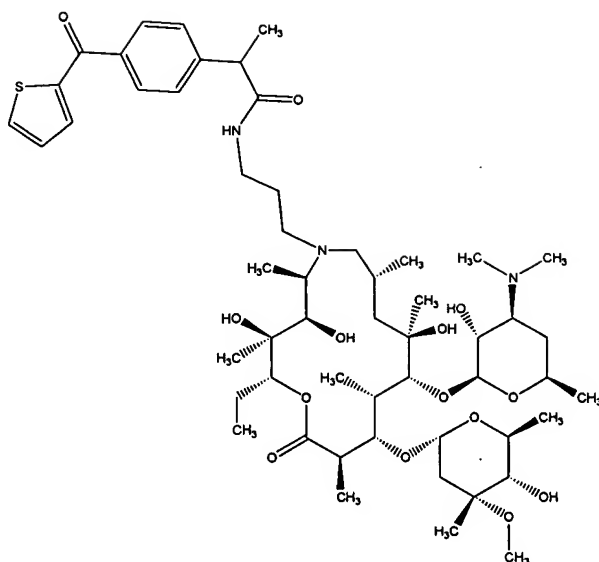
and ~~pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

26. (Currently Amended) A compound of the formula



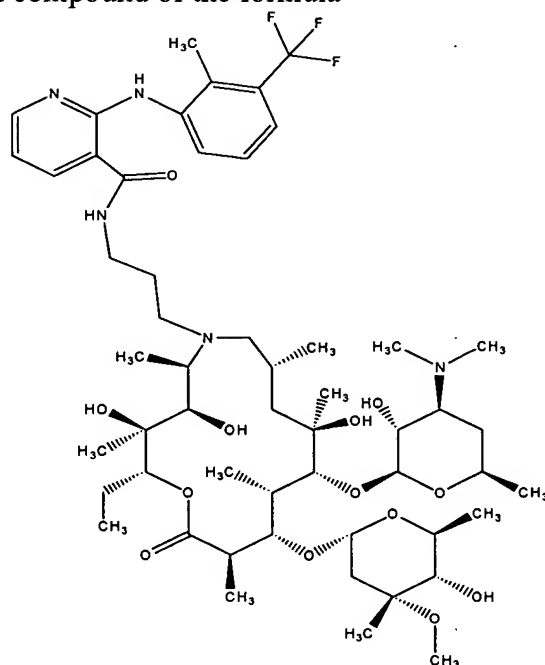
and ~~pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

27. (Currently Amended) A compound of the formula



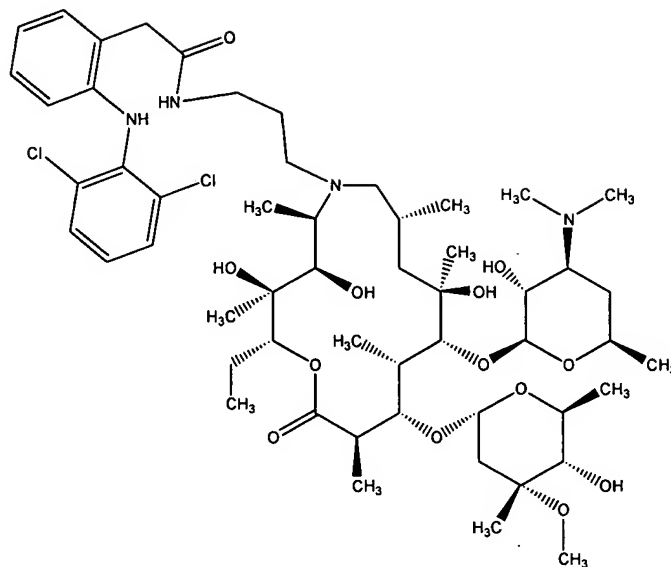
and ~~pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

28. (Currently Amended) A compound of the formula



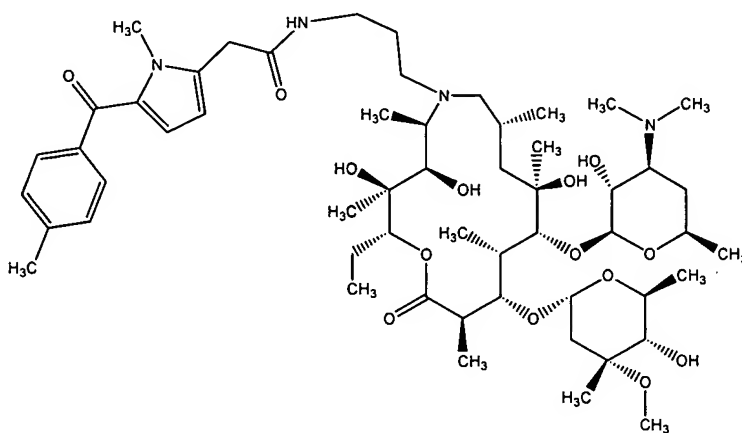
and ~~pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

29. (Currently Amended) A compound of the formula



and pharmaceutically acceptable salts and solvates thereof or a pharmaceutically acceptable salt or solvate thereof.

30. (Currently Amended) A compound of the formula

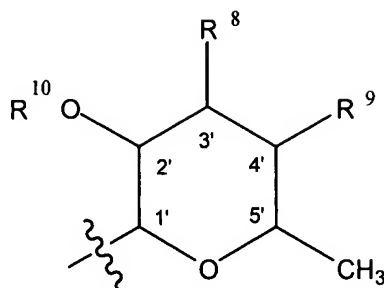


and pharmaceutically acceptable salts and solvates thereof or a pharmaceutically acceptable salt or solvate thereof.

31. (Currently Amended) A process for the preparation a compound of Formula I

R¹ is hydroxy, OR^p, -O-S² group or an =O;

S¹ is a sugar moiety of formula:



wherein

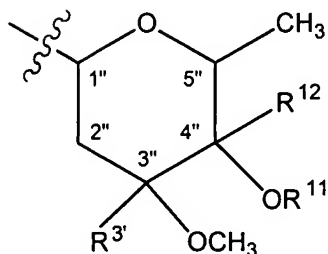
R⁸ and R⁹ are both hydrogen or together form a bond, or R⁹ is hydrogen and R⁸ is -

$\text{N}(\text{CH}_3)\text{R}^y$, wherein

R^y is R^p, R^z or -C(O)R^z wherein R^z is hydrogen or alkyl or alkenyl or alkynyl or cycloalkyl or aryl or heteroaryl or alkyl substituted with C₂-C₇-alkyl, C₂-C₇-alkenyl, C₂-C₇-alkynyl, aryl or heteroaryl

R^{10} is hydrogen or R^p ;

S² is a sugar moiety of formula :



wherein:

R³' is hydrogen or methyl;

R^{11} is hydrogen, R^p or $O-R^{11}$ is a group that with R^{12} and with C/4" carbon atom forms a $>C=O$ or epoxy group;

R¹² is hydrogen or a group that with O-R¹¹ group and with C/4" carbon atom forms a >C=O or epoxy group;

R² is hydrogen, hydroxy, OR^p or alkoxy;

A is hydrogen or methyl;

B is methyl or epoxy;

E is hydrogen or halogen;

R^3 is hydroxy, OR^p , alkoxy or R^3 is a group that with R^5 and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate; or if W or Z is $>N-R_N$ R^3 is a group that with W or Z forms a cyclic carbamate;

R^4 is C_1 - C_4 alkyl;

R^5 is hydrogen, hydroxy, OR^p , C_1 - C_4 -alkoxy, or a group that with R^3 and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate;

R^6 is hydrogen or C_1 - C_4 -alkyl;

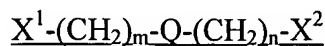
wherein **M** has a linkage site through which it is linked to **D** *via* linking group **L**; provided that the linkage site being at one or more of the following:

- any reactive hydroxy, nitrogen, or epoxy group located on S^1 , S^2 , or an aglycone oxygen if S^1 or/and S^2 is cleaved off;
- a reactive $>N-R_N$ or $-NR_tR_s$ or $=O$ group located on Z or W;
- a reactive hydroxy group located at any one of R^1 , R^2 , R^3 , and R^5 ;
- any other group that can be first derivatized to a hydroxy or $-NR_tR_s$ group and

R^p is hydroxyl or amino protective group;

wherein **L** represents a group of

Formula IV:



IV

wherein

X^1 is selected from: $-CH_2-$, $-C(O)-$, $OC(O)-$, $N-O-$ or $-OC(O)NH-$, $-C(O)NH-$;

X² is -NH- or -NHC(O)-, -OC(O)-, -C(O)-, -O or -CH₂-;

Q is -NH- or -CH₂-, or absent;

wherein each -CH₂- or -NH- group may be optionally substituted by C₁-C₇-alkyl,

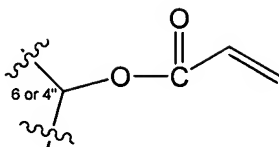
C₂-C₇-alkenyl, C₂-C₇-alkynyl, C(O)R^x, C(O)OR^x, C(O)NHR^x wherein R^x is C₁-C₇-alkyl, aryl or heteroaryl;

the symbols m and n independently are a whole number from 0 to 4, with the proviso that if Q is NH, n cannot be 0

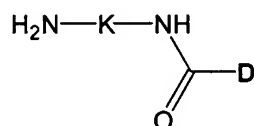
D is derived from the NSAIDs selected from the group consisting of: aceclofenac, acemetacin, acetaminophen, acetaminosalol, acetyl-salicylic acid, acetyl-salicylic-2-amino-4-picoline-acid, 5-aminoacetylsalicylic acid, alclofenac, aminoprofen, amfenac, ampyrone, ampiroxicam, anileridine, bendazac, benoxaprofen, bermoprofen, α -bisabolol, bromfenac, 5-bromosalicylic acid acetate, bromosaligenin, bucloxic acid, butibufen, carprofen, celexocib, chromoglycate, cinmetacin, clindanac, clopirac, sodium diclofenac, diflunisal, ditazol, droxicam, enfenamic acid, etodolac, etofenamate, felbinac, fenbufen, fenclozic acid, fendosal, fenoprofen, fentiazac, fepradinol, flufenac, flufenamic acid, flunixin, flunoxaprofen, flurbiprofen, glutametacin, glycol salicylate, ibufenac, ibuprofen, ibuproxam, indomethacin, indoprofen, isofezolac, isoxepac, isoxicam, ketoprofen, ketorolac, lornoxicam, loxoprofen, meclofenamic acid, mefenamic acid, meloxicam, mesalamine, metiazinic acid, mofezolac, montelukast, nabumetone, naproxen, niflumic acid, nimesulide, olsalazine, oxaceprol, oxaprozin, oxyphenbutazone, paracetamol, parsalmide, perisoxal, phenyl-acethyl-salicylate, phenylbutazone, phenylsalicylate, pyrazolac, piroxicam, pirprofen, pranoprofen, protizinic acid, reserveratol, salacetamide, salicylamide, salicylamide-O-acetyl acid, salicylsulphuric acid, salicin, salicylamide, salsalate, sulindac, suprofen, suxibutazone, tamoxifen, tenoxicam, tiaprofenic acid, tiaramide, ticlopridine, tinoridine, tolfenamic acid, tolmetin, tropesin, xenbucin, ximoprofen, zaltoprofen, zomepirac, tomoxiprol, zafirlukast and cyclosporin;
~~**L** is a linker molecule to which each of **M** and **D** are covalently linked;~~

which comprises:

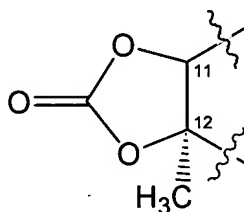
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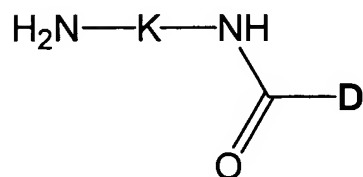
and a free amino group of the compound represented by formula :



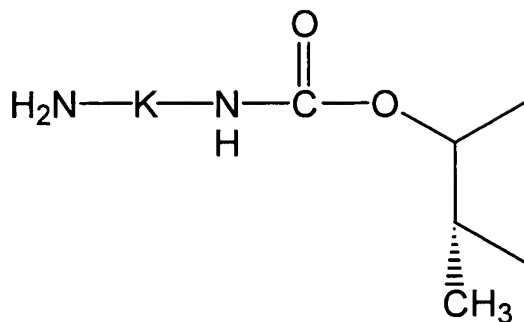
d) for a compound of Formula I, where X^1 is $-\text{OC}(\text{O})\text{NH}-$ and X^2 is $-\text{NHC}(\text{O})-$, by reacting a macrolide represented by formula



and free amino group of of the compound represented by formula:

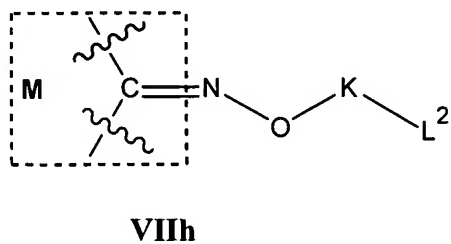
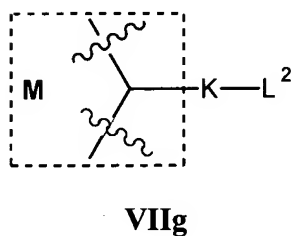
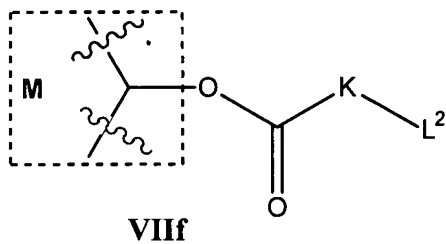


e) for a compound of Formula I, where X^1 is $-\text{CH}_2-$, Q is $-\text{NH}-$ and X^2 is $-\text{NHC}(\text{O})-$, by reacting a macrolide represented by formula:



and a compound of Formula V;

f) for a compound of Formula I by reacting a macrolide represented by Formula **VIIIf** or by Formula **VIIg** or by Formula **VIIh** having a leaving group L^2



with a free carboxylic acid of nonsteroidal anti-inflammatory subunit.

32. (Previously Presented) A pharmaceutical composition comprising a compound according to claim 1 as well as a pharmaceutically acceptable diluent or carrier.

33. (Currently Amended) A method of treating inflammatory diseases, disorders ~~and~~ or conditions characterized by or associated with an undesirable inflammatory immune response, and all diseases and conditions induced by or associated with an excessive secretion of TNF- α and IL-1 which comprises administering to a subject in need of treatment a therapeutically effective amount of a compound according to claim 1.

34. (Currently Amended) A method of treating inflammatory conditions ~~and~~ or immune or anaphylactic disorders associated with infiltration of leukocytes into inflamed tissue in a subject in need thereof which comprises administering to said subject a therapeutically effective amount of a compound according to claim 1.

35. (Previously Presented) The method according to claim 34, wherein inflammatory conditions and immune disorders are selected from the group consisting of asthma, adult respiratory distress syndrome, bronchitis, and cystic fibrosis.

36. (Previously Presented) A method according to claim 34, wherein said inflammatory conditions and immune disorders are selected from the group consisting of inflammatory conditions or immune disorders of the lungs, joints, eyes, bowel, skin, and heart.

37. (Previously Presented) A method according to claim 34, wherein said inflammatory conditions and immune disorders are selected from the group consisting of asthma, adult respiratory distress syndrome, bronchitis, cystic fibrosis, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, uveitis, conjunctivitis, inflammatory bowel conditions, Crohn's

